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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/723,361	11/26/2003	Yizhong Gu	PB0105	1196

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EXAMINER	
STEADMAN, DAVID J	

ART UNIT	PAPER NUMBER
1656	

DATE MAILED: 09/05/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/723,361	GU ET AL.	
	Examiner	Art Unit	
	David J. Steadman	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 June 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *21-28,30-32,35-42,45-47,50-52,55 and 57-61* is/are pending in the application.

4a) Of the above claim(s) *23-28,30-32,36-42,46,47,51,52,55 and 61* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *21,22,35,45,50 and 57-60* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. 09/866,108.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *11/26/03*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: Appendices A, B

DETAILED ACTION

Status of the Application

[1] Claims 21-28, 30-32, 35-42, 45-47, 50-52, 55, and 57-61 are pending in the application.

[2] Applicant's amendment to the claims, filed on 6/23/2006, is acknowledged. This listing of the claims replaces all prior versions and listings of the claims.

[3] Applicant's amendment to the specification, filed on 6/23/2006, is acknowledged.

Election/Restriction

[4] Applicant's election without traverse of Group I, claims 21-22, 35, 45, 50, and 57-60, in the reply filed on 6/23/2006 is acknowledged.

[5] Claims 23-28, 30-32, 36-42, 46-47, 51-52, 55, and 61 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim.

Priority

[6] Applicant's claim to domestic priority under 35 USC § 119(a)-(d), § 119(e) and § 120 is acknowledged. In order to expedite examination of the instant application, the examiner requested (in the prior Office action) applicant to identify the priority application(s) that discloses the claimed sequence. In response, applicant states for the record that priority applications 09/866,108 and 60/266,860 disclose the claimed

invention. See instant response at p. 12. Thus, the instant application has an earliest effective filing date of 2/5/2001.

Information Disclosure Statement

[7] All references cited in the IDS filed on 11/26/2003 have been considered by the examiner. A copy of Forms PTO-1449 is attached to the instant Office action.

Specification/Informalities

[8] The specification is objected to as the status of referenced applications has not been updated. Applicant should review the specification and update the status of applications mentioned therein. See, *e.g.,* p. 150, line 7 and p. 158, line 5 of the instant specification.

Claim Rejections - 35 USC § 112, Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

[9] Claims 21 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 21 is drawn to "[a]n isolated polypeptide..." (emphasis added). According to a dictionary definition, "isolated" means to "to set apart from others" or "to select from among others; *especially* : to separate from another substance so as to obtain pure or

in a free state" (see Appendix A). In view of this definition, the claim is confusing as there is no indication in the active method steps of the claim that the polypeptide has been separated from others that are expressed by the host cell, *i.e.,* it would appear from the recited active method steps that the polypeptide produced thereby is not isolated. It is suggested that applicant clarify the meaning of the claim.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:
Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

[10] Claims 21-22, 35, 45, 50, and 57-60 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or well-established utility. The claims are drawn to SEQ ID NO:3 and variants thereof, a pharmaceutical composition, a diagnostic composition and a fusion protein.

The specification discloses SEQ ID NO:3 is a "a human myosin-like protein" (specification at p. 8, middle) or a "human myosin heavy chain-like protein" (specification at p. 15, bottom). According to the specification, defects in SEQ ID NO:3 function and/or expression contribute to human disease (p. 164, bottom) and SEQ ID NO:3 is useful in diagnosis, prevention, or treatment of disorders (specification at p. 15, bottom). However, there is no evidence of record that the polypeptide of SEQ ID NO:3 is a defective polypeptide, is associated with or contributes to human disease, or can be used to diagnose, prevent, or treat a disorder. Thus, without further experimentation, one of skill in the art would not be able to use the claimed polypeptide for these uses.

This type of utility is not considered a "substantial utility". See e.g., *Brenner v. Manson,* 383 U.S. 519, 148 USPQ 689 (Sup. Ct. 1966). The specification must teach a skilled artisan how to use what is claimed and not merely provide a blueprint for further experimentation in order for an artisan to identify a use for the claimed invention.

[11] Claims 21-22, 35, 45, 50, and 57-60 also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial utility asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Claim Rejections - 35 USC § 112, First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

[12] Claims 21-22, 35, 45, 50, and 57-60 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

Claims 21 and 22 (claims 35, 45, 50, and 57-60 dependent therefrom) are drawn to (in relevant part) a genus of polypeptide variants of SEQ ID NO:3, wherein the polypeptide can have any function.

For claims drawn to a genus, MPEP § 2163 states the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. MPEP § 2163 states that a representative number of species means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus. In this case, the specification discloses only a single representative species of the claimed genus of polypeptides, *i.e.*, SEQ ID NO:3. The specification fails to describe any additional representative species of the claimed genus of nucleic acids. While MPEP § 2163 acknowledges that in certain situations "one species adequately supports a genus," it also acknowledges that "[f]or inventions in an unpredictable art, adequate written description of a genus which embraces widely variant species cannot be achieved by disclosing only one species within the genus." In the instant case, the claimed genus of polypeptides encompasses species that are widely variant in their structures and

functions. As such, the disclosure of the single representative species as noted above is insufficient to be representative of the attributes and features of all species of polypeptides as encompassed by the claims.

Given the lack of description of a representative number of polypeptides, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicant was in possession of the claimed invention.

[13] Claims 21-22, 35, 45, 50, and 57-60 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for SEQ ID NO:3 and a composition thereof, does not reasonably provide enablement for all variants of SEQ ID NO:3 having any activity/function as broadly encompassed by the claims and pharmaceutical and diagnostic compositions thereof. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

It is the examiner's position that undue experimentation is required for a skilled artisan to make and/or use the entire scope of the claimed invention. Factors to be considered in determining whether undue experimentation is required are summarized in *In re Wands* (858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)) as follows: (A) The breadth of the claims; (B) The nature of the invention; (C) The state of the prior art; (D) The level of one of ordinary skill; (E) The level of predictability in the art; (F) The amount of direction provided by the inventor; (G) The existence of working examples;

and (H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure. See MPEP § 2164.01(a). MPEP 2164.04 states, "[w]hile the analysis and conclusion of a lack of enablement are based on the factors discussed in MPEP § 2164.01(a) and the evidence as a whole, it is not necessary to discuss each factor in the written enablement rejection" and that "[t]he language should focus on those factors, reasons, and evidence that lead the examiner to conclude that the specification fails to teach how to make and use the claimed invention without undue experimentation, or that the scope of any enablement provided to one skilled in the art is not commensurate with the scope of protection sought by the claims." Accordingly, the Factors most relevant to the instant rejection are addressed in detail below.

The breadth of the claims: Claims 21 and 22 (claims 35, 45, 50, and 57-60 dependent therefrom) are drawn to (in relevant part) structural and functional variants of SEQ ID NO:3, including a polypeptide encoded by a complement of a SEQ ID NO:3-encoding nucleic acid. It is also noted that claim 21 recites "culturing a host cell, or the progeny thereof..." According to the specification, "the invention provides transgenic cells and non-human organisms comprising hGDMLP-1 nucleic acids...The cells can be embryonic stem cells" (specification at p. 137, lines 2-7), thus the claims encompass polypeptide that is produced by transgenic embryonic stem cells, including organs and tissues that are considered to be "progeny thereof." Claim 35 is drawn to a "pharmaceutical composition" comprising the polypeptide of claim 22. The term "pharmaceutical" has been given patentable weight, implying a therapeutic use of the claimed "pharmaceutical composition." Similarly, the term "diagnostic" in claims 45 and

50 has been given patentable weight, implying a diagnostic use of the claimed "diagnostic composition." The enablement provided by the specification is not commensurate in scope with the claims with regard to the number of polypeptides encompassed by claims 21 and 22 and compositions encompassed by claims 35, 45, and 50. In this case, the specification is enabling only for SEQ ID NO:3 and a composition thereof.

The state of the prior art; The level of one of ordinary skill; and The level of predictability in the art: Regarding the polypeptides of claims 21 and 22, the amino acid sequence of a polypeptide determines the its structural and functional properties. Predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity/utility requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (*i.e.*, expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. The positions within a protein's sequence where modifications can be made with a reasonable expectation of success in obtaining a polypeptide having the desired activity/utility are limited in any protein and the result of such modifications is highly unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, *e.g.*, multiple substitutions. While one may argue that certain of the variants of SEQ ID NO:3 are limited to those having "conservative amino acid substitutions" or "moderately conservative amino acid substitutions," even such "conservative" substitutions can have significant effects on the

function of a polypeptide, given the high level of unpredictability in modifying the amino acid sequence of a polypeptide. At the time of the invention, methods for isolating or generating variants and mutants of a given polypeptide were known in the art. However, neither the specification nor the state of the art at the time of the invention provided the necessary guidance for altering the polypeptide of SEQ ID NO:3 with an expectation of obtaining a polypeptide having the desired activity/utility. At the time of the invention, there was a high level of unpredictability associated with altering a polypeptide sequence with an expectation that the polypeptide will maintain the desired activity/utility. For example, the reference of Witkowski et al. (*Biochemistry* 38:11643-11650, 1999) teaches that only a single amino acid substitution results in conversion of the activity of a polypeptide to a second, distinct activity (see *e.g.*, Table 1, page 11647).

Regarding the polypeptide produced by transgenic cells, including organs and tissues that are considered to be "progeny thereof" as encompassed by claim 21, it is noted that it is highly unpredictable as to whether a transgenic cell can be used to produce "progeny" organs and tissues. For example, the reference of Hipp et al. (*J. Exp. Clin Assist Reprod.* 1:1-10, 2004) teaches that a kidney is "one of the most difficult organs to reconstruct" (p. 4, right column, top).

The amount of direction provided by the inventor and The existence of working examples: Regarding the polypeptides of claims 21-22, the specification discloses only a single working example of the claimed polypeptide, *i.e.,* SEQ ID NO:3. The specification fails to disclose any specific guidance for altering the polypeptide of SEQ

ID NO:3 with an expectation that the polypeptide variant will maintain the desired activity/utility. Furthermore, the specification fails to provide any guidance for using those polypeptides that do not maintain the desired activity/utility, *e.g.*, non-functional polypeptides – particularly the polypeptide that is encoded by the "complement of the nucleotide sequence of any one of (i) – (vi)."

Regarding the polypeptide produced by transgenic cells, including organs and tissues that are considered to be "progeny thereof" as encompassed by claim 21, the specification fails to provide a single working example of an embryonic stem cell transfected with a SEQ ID NO:3-encoding nucleic acid or guidance thereof such that one of skill in the art could generate "progeny" thereof, including a tissue or organ as encompassed by the claims.

Regarding the "pharmaceutical" and "diagnostic" compositions of claims 35, 45, and 50, the specification fails to provide a working example of a disease/disorder/condition that can be treated or diagnosed using the polypeptide of SEQ ID NO:3 or variants thereof as encompassed by the claims or specific guidance for treating or diagnosing a disease/disorder/condition.

The quantity of experimentation needed to make or use the invention based on the content of the disclosure: While methods of isolating and/or generating variants of a polypeptide were known in the art at the time of the invention, it was not routine in the art to screen – by a trial and error process – for all polypeptides having a substantial number of modifications as encompassed by the claims for those that maintain the desired activity/utility. Further, it was not routine in the art at the time of the invention to

generate all transgenic tissues and organs as encompassed by the claims. Also, it was not routine to experiment to determine those diseases/disorders/conditions that – if at all possible – can be treated or diagnosed using SEQ ID NO:3 or a variant thereof as encompassed by the claims.

In view of the overly broad scope of the claims, the lack of guidance and working examples provided in the specification, the high level of unpredictability as evidenced by the prior art, and the amount of experimentation required, undue experimentation is necessary for a skilled artisan to make and use the entire scope of the claimed invention. Applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims. The scope of the claims must bear a reasonable correlation with the scope of enablement (*In re Fisher*, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See *In re Wands* 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

[14] Claim(s) 22, 35, 45, 50, and 57-58 are rejected under 35 U.S.C. 102(b) as being anticipated by Lehner et al. (WO 96/23886). The claims are drawn to variants of SEQ ID NO:3, a pharmaceutical composition thereof, a diagnostic composition thereof, and a fusion protein.

The reference of Lehner et al. teaches a polypeptide, SEQ ID NO:9 at p. 44, that comprises 8 contiguous amino acids of SEQ ID NO:3 herein (Appendix B). Lehner et al. further teaches the polypeptide may be in the form of a fusion protein fused to an antigenic polypeptide such as heterologous T- or B-cell epitopes (p. 11, bottom), which has been interpreted as being a "diagnostic composition" that is diagnostic of the presence of and can be detected by a cognate T- or B-cell antibody. Lehner et al. teaches the polypeptide may be in the form of a pharmaceutical composition for treatment of dental caries (p. 17, bottom). This anticipates claims 22, 35, 45, 50, and 57-58 as written.

Examiner Comment/Clarification

[15] "[A] nucleotide sequence that is a degenerate variant of the nucleotide sequence of SEQ ID NO:2" has been interpreted by the examiner as meaning a variant of SEQ ID NO:2, that, due to degeneracy of the genetic code, necessarily encodes SEQ ID NO:3. See specification at p. 18, lines 10-15.

Conclusion

[16] Status of the claims:

- Claims 21-28, 30-32, 35-42, 45-47, 50-52, 55, and 57-61 are pending.
- Claims 23-28, 30-32, 36-42, 46-47, 51-52, 55, and 61 are withdrawn from consideration.
- Claims 21-22, 35, 45, 50, and 57-60 are rejected.
- No claim is in condition for allowance.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David J. Steadman whose telephone number is 571-272-0942. The examiner can normally be reached on Mon to Fri, 7:30 am to 4:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Kathleen Kerr can be reached on 571-272-0931. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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Art Unit 1656